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1. Fried

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Nov. 13, '92

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Summary

Page No. 41

**Assistant Commissioner for Patents
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US005851999A

United States Patent [19][11] **Patent Number:** **5,851,999****Ullrich et al.**[45] **Date of Patent:** **Dec. 22, 1998**[54] **FLK-1 IS A RECEPTOR FOR VASCULAR
ENDOTHELIAL GROWTH FACTOR**[56] **References Cited**[75] **Inventors:** Axel Ullrich, München; Werner Risau,
Grafelfing; Birgit Millauer, München,
all of Germany; Aviv Gazit; Alex
Levitaki, both of Jerusalem, Israel**PUBLICATIONS**

Ueno et al (1991) Science 252: 844-848.

Ueno et al (1992) J. Biol. Chem. 267: 1470-1476.

[73] **Assignees:** Max-Planck-Gesellschaft zur
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the Hebrew University of Jerusalem,
Jerusalem, Israel*Primary Examiner*—Bruce R. Campell
Attorney, Agent, or Firm—Pennie & Edmonds LLP[57] **ABSTRACT**

The present invention relates to the use of ligands for the FLK-1 receptor for the modulation of angiogenesis and vasculogenesis. The invention is based, in part, on the demonstration that Flk-1 tyrosine kinase receptor expression is associated with endothelial cells and the identification of vascular endothelial growth factor (VEGF) as the high affinity ligand of Flk-1. These results indicate a major role for Flk-1 in the signaling system during vasculogenesis and angiogenesis. Engineering of host cells that express Flk-1 and the uses of expressed Flk-1 to evaluate and screen for drugs and analogs of VEGF involved in Flk-1 modulation by either agonist or antagonist activities is described. The invention also relates to the use of FLK-1 ligands, including VEGF agonists and antagonists, in the treatment of disorders, including cancer, by modulating vasculogenesis and angiogenesis.

[21] **Appl. No.:** 443,861[22] **Filed:** May 22, 1995**Related U.S. Application Data**[60] Division of Ser. No. 193,829, Feb. 9, 1994, which is a
continuation-in-part of Ser. No. 38,596, Mar. 26, 1993,
abandoned, which is a continuation-in-part of Ser. No.
973,750, Nov. 13, 1992, abandoned.[51] **Int. Cl.⁶** A61K 48/00; C12N 5/00;
C12N 15/00[52] **U.S. Cl.** 514/44; 424/93.2; 435/320.1[58] **Field of Search** 514/44; 435/69.1,
435/172.3, 320.1, 252-3, 361, 375; 424/93.2;
935/57, 70, 71, 32**32 Claims, 25 Drawing Sheets**